

the 7 isomer. Recrystallization of the product from EtOH yielded 4.0 g of white needles, mp 187.0–188.0°. *Anal.* (C<sub>13</sub>H<sub>13</sub>BrNO<sub>2</sub>) C, H, Br, N.

**5-Carbomethoxy-2-ethyldecahydroisoquinoline Hydrobromide.**—5-Carbomethoxy-2-ethyl-1,2,3,4-tetrahydroisoquinoline (1 g), AcOH (30 ml), and concentrated H<sub>2</sub>SO<sub>4</sub> (0.1 ml) were hydrogenated (PtO<sub>2</sub>, 1 g, 48 hr, 3.52 kg/cm<sup>2</sup>). The product was isolated in the usual manner, and the hydrobromide salt was prepared and recrystallized (EtOH–Et<sub>2</sub>O) (0.3 g, mp 168.0–169.0°). The uv spectrum of this compound showed no absorption in the range 220–360 mμ. *Anal.* (C<sub>13</sub>H<sub>24</sub>BrNO<sub>2</sub>) C, H, Br, N.

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### Diimides of Cyclobutane-1,1-dicarboxylic Acid<sup>1a</sup>

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Various imides of cyclobutanecarboxylic acid, particularly N-acetylcyclobutanecarboxamide, possess a structure-dependent ability to act as central nervous system depressants.<sup>2</sup> The phenomenon appears to be related to the cyclobutane ring system and is unique in that it is not subject to circadian rhythm variance, a finding contrary to the behavior of barbiturates. To further elucidate the biochemistry of cyclobutane compounds we have expanded the original study to a group of cyclobutane-1,1-dicarboxylic acid derivatives. With the exception of **6**, a spirothiobarbiturate, these substances are di-N-acylimides and congeners of the compounds studied earlier.

When bioassayed the compounds were tested as reported previously<sup>2</sup> but dispersed in mineral oil, since they tended to agglomerate when ground in 0.25% methylcellulose. At a dose of 1000 mg/kg there was no loss of spontaneous activity nor were there any deaths. In addition to intraperitoneal administration, the compounds were also given orally as suspensions in gum tragacanth with the same lack of effect.

They were also tested as potentiators of barbiturate sedation<sup>3,4</sup> using pentobarbital sleeping time, judged by loss of the righting reflex, as a criterion. Using five mice and 50-mg/kg ip dose of the barbiturate, a mean sleeping time of 81 min was obtained. The only compound exhibiting potentiation was **6**. The mean sleeping time for five mice receiving 500 mg/kg of this compound orally 30 min before the standard dose of barbiturate was 147 min. A potentiation factor of 1.8 on the part of this compound at a dose which itself appears to have no depressant activity is of considerable practical and mechanistic interest.

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### Experimental Section

Microanalyses were performed by Midwest Microlab, Inc., Indianapolis, Ind.

**Preparation of Diimides.**—A mixture of 20 g of SOCl<sub>2</sub> and 5 g (0.034 mole) of cyclobutane-1,1-dicarboxylic acid was refluxed for 1.5 hr (hood) and excess SOCl<sub>2</sub> was removed by flash evaporation. Crude cyclobutane-1,1-dicarbonyl chloride (1.6 g, 0.009 mole) was added dropwise to a stirred and cooled solution of the amide (0.018 mole) in 10 ml of neutral alumina washed and KOH-dried pyridine. In every case an exothermic reaction ensued; when it subsided the mixture was heated on the steam bath for 1 hr. The reaction mixture was then poured onto 100 g of crushed ice and the product precipitated. Solvents used in crystallization and yields of the respective compounds are in Table I.

TABLE I

DIIMIDES OF CYCLOBUTANE-1,1-DICARBOXYLIC ACID

No.	R	Yield, %	Mp, °C <sup>a</sup>	Crystn <sup>b</sup> solvent	Formula	Analysis <sup>c</sup>
1	CH <sub>3</sub>	40	215	C	C <sub>10</sub> H <sub>14</sub> N <sub>2</sub> O <sub>4</sub>	N
2	C <sub>2</sub> H <sub>5</sub>	50	243	A	C <sub>12</sub> H <sub>18</sub> N <sub>2</sub> O <sub>4</sub>	N
3	C(CH <sub>3</sub> ) <sub>3</sub>	60	215	A	C <sub>16</sub> H <sub>26</sub> N <sub>2</sub> O <sub>4</sub>	N
4	(CH <sub>2</sub> ) <sub>4</sub> CH <sub>3</sub>	50	175	E	C <sub>18</sub> H <sub>30</sub> N <sub>2</sub> O <sub>4</sub>	N
5		45	255	A	C <sub>16</sub> H <sub>22</sub> N <sub>2</sub> O <sub>4</sub>	N
6	>C=S	40	220	C	C <sub>7</sub> H <sub>8</sub> N <sub>2</sub> O <sub>2</sub> S	C, H, N

<sup>a</sup> Corrected. <sup>b</sup> A, acetone; B, benzene; C, chloroform; E, ethyl ether. <sup>c</sup> Analytical results obtained for the elements listed were within ±0.4% of the theoretical values.

### Imidothiazoles

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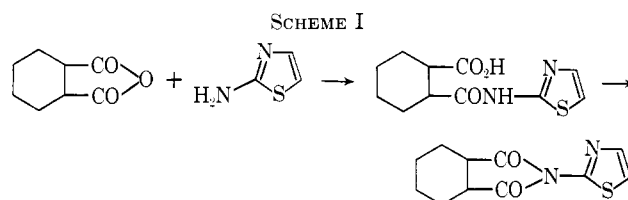
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As part of a continuing study of various imides<sup>2–4</sup> and their reduction products as pharmacologically active compounds, we have prepared a limited series of imides derived from 2-aminothiazole and related thiazoles. These imides were obtained from a wide variety of compounds of diverse structure. An example employing 1,2-cyclohexanedicarboxylic anhydride illustrates the general method used (Scheme I). This reaction was either accomplished by heating an intimate



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